

# What belongs in the next chapter . . .

## *A letter from the Executive Director*

*AVAC Report 2010: Turning the Page*, marks 15 years of AVAC's advocating and agitating, watching and waiting, for the end of AIDS.

Are we there yet? No, but the AIDS vaccine field can at last say that it is closer. The Thai Prime-Boost trial known as RV144 provided the first evidence in humans that a vaccine can protect against HIV. As we discuss in the pages that follow, there is a vast array of caveats, questions and next steps that the field has to tackle.

But before you turn this page, we want to reiterate some of the top-line messages about RV144 that must be shared outside the small world of AIDS vaccine research:



**Many media, many messages** From left to right : A community discussion of the Thai Prime-Boost trial in Rayong City, Thailand; global news coverage of the Thai trial result; young men learning about medical male circumcision for HIV prevention in Uganda. [Thai photos courtesy of Tom Paulson, Ugandan photo courtesy of US Military HIV Research Program]

- Prevention of HIV via a vaccine is possible.
- An AIDS vaccine is as urgently needed as it has ever been.
- A partially protective vaccine would be a powerful tool for controlling the epidemic. RV144 data suggest that the vaccine reduced HIV risk by around 30 percent. This is lower than the threshold the trial team set with the Thai government for pursuing vaccine licensure. But this doesn't mean—as some observers have suggested—that *any* vaccine providing moderate protection would be useless.
- The results obtained to date by the AIDS vaccine field are evidence of what enthusiastic community support for a study can achieve—and are the reason why communities should continue to partner in trials.
- Pre-exposure prophylaxis (PrEP), microbicides, treatment as prevention and proven strategies like male and female condoms and male circumcision are part of the “big picture” of AIDS vaccine research. Stakeholders working within the AIDS vaccine field know that combination prevention is key. There will be no silver bullet for HIV prevention.

The Thai Prime-Boost trial announced its results in September and October of last year. Now that the dust has settled, it's clear that the messages listed on the previous page have barely taken hold for much of the general public. In conversations with advocates, frontline HIV treatment providers and even staff at other clinical trial sites, we have encountered confusion about the trial and its results. Some people believe that the vaccine succeeded and now exists in Thailand. Others think it failed completely.

The truth, of course, is somewhere in between. There is a glimmer of hope that has to be followed. Sometimes a glimmer is enough; sometimes it is the only sign of the bright day to come. At AVAC, we're not convinced that RV144 is going to lead the AIDS vaccine field to a preventive vaccine—but we are convinced that the result is a substantive lead. How the field communicates about and acts on this result is absolutely critical to future work on AIDS vaccines.

With its data on efficacy, RV144 generated momentum that never existed before. There is no telling what will come from aggressive pursuit of the result—but that is the nature of science. This is the bottom line message that should be communicated loudly and clearly to the general public and key stakeholders, including policy makers, political and community leaders, civil society advocates and activists and others.

The effort to follow up on the Thai trial result must be a priority. There should be a clear, coordinated and well-funded plan jointly developed and executed in the collaborative spirit that animated the Global HIV Vaccine Enterprise at its inception.

At the same time, the field has to pursue other options. Whether the RV144 clues lead to an effective candidate or not, there will be a need for further improvements and/or wholly novel approaches.

In other words, the AIDS vaccine field needs to further explore the RV144 result *and* pursue unique

approaches. And it needs to do this in the context of constrained resources.

Today, there are yawning gaps in funding for proven prevention and treatment and a crisis in political will supporting AIDS programs. Those of us working on the AIDS epidemic face skepticism about whether disease-specific funding for AIDS is cost effective. Those of us working on AIDS vaccines face skepticism about whether limited funds for AIDS should include funding for AIDS prevention research.

We hope that the next chapter of AIDS vaccine research shows the field to be capable of triaging current projects—jettisoning some, streamlining others, scaling up still others—and developing a clear strategy for collaborative action on key goals. The field must be able to define how it will function in the absence of new funding and how additional resources would be spent, if they became available.

It's easy to call for all of these things and much, much harder to achieve them. The pages that follow contain our best suggestions for how to do so.

In **Chapter One: “Proof of Concept” and its Consequences**, we propose some guiding principles for the post-RV144 scientific agenda.

In prevention research, scientific breakthroughs cannot be achieved without the participation of trial participants and their immediate and national communities. To take the full measure of community engagement undertaken for the Thai Prime-Boost trial, AVAC commissioned award-winning reporter Tom Paulson to travel to Thailand and interview many of the trial staff and advocates who were closest to the process. The result is **Chapter Two: The Thai Way Forward**, a thought-provoking look at what worked and what didn't work in the world's largest AIDS vaccine trial to date.

In any budget crunch, it's critical to do more with what is already available. For the AIDS vaccine field and for HIV prevention research in general,

this means doing as much as possible with the information gleaned from trials. In **Chapter Three: Data and Materials—A “to do” list for the future**, we look at some of the essential steps to optimize the value of samples and data from clinical trials.

While the first three chapters in the Report have a specific vaccine focus, the reality is that the next big results are going to come from trials of ARV-based prevention—both topical microbicide gels and oral PrEP. Whether these results are positive, flat or indeterminate, they’ll be big in the sense that they’ll raise tricky and important questions about what to do with the results and what trials are needed next. **Chapter Four: Trials and Trial Design—Where does prevention research go from here?** zeroes in on some of the key issues emerging in discussions of next-generation trials.

**The report’s conclusion, Speak with one voice, work towards one goal**, weighs the impact of developments in ARV-based prevention, debates around “test-and-treat”, and treatment shortages on the global AIDS response.

This year’s report is titled *Turning the Page* because we see the Thai trial result as starting a new chapter for AIDS vaccine and prevention research. These are some of the things we hope will be part of the next chapter:

- A balance between focused investigation to better understand the Thai trial result and its implications for further vaccine development, and ongoing basic scientific work exploring other potential directions for vaccine design and development.
- Clinical trials that are innovative in how they collect, analyze and act upon data. This might include adaptive trial designs that allow analysis and adjustments while the study is still ongoing.
- More extensive and better-funded community engagement than ever before. This is essential as

## We Are All Advocates

One of the founding principles of AVAC is that scientists and civil society members need to work together to set, and implement, a single agenda. Scientists can be “community”. Civil society can be technical experts. And we all belong at the table together, facing the challenges of the epidemic head on. Simply put, we are all advocates. What does this mean? What, exactly, does advocacy look like? Throughout the pages of this year’s Report, you’ll find exciting perspectives from a range of individuals who hail from different parts of the world and work in a variety of professions—all working toward the goal of ending AIDS.

the field seeks support for and participation in trials with increasingly complicated designs.

- Approaches to gathering and sharing data that are cutting-edge, collaborative and that cut across disciplines. These are needed to optimize the information gleaned from trials of AIDS vaccines and of other prevention strategies.
  - An AIDS vaccine field that adapts to emerging results from other biomedical prevention trials, like pre-exposure prophylaxis (PrEP) and microbicides, by preparing for positive data with new ideas for trial design and combination prevention.
  - Better answers about if, when, how and to whom a partially effective product would be introduced. This goes for AIDS vaccines, PrEP, microbicides *and* male circumcision.
  - A biomedical prevention research field that invests as much in socio-behavioral research and community partnership to understand and define participants’ risk before, during and after a trial, as it does in scientific evaluation of prospective candidates.
- The African American poet and author Maya Angelou writes, “History, despite its wrenching pain, cannot be unlived, but if faced with courage, need not be lived again.” As we’ve spent the past

several months preparing this year's Report and contemplating the next chapter of AIDS vaccine research, we've also looked back.

It's not possible to unlive the tumultuous decision-making, budget-cutting and protocol-editing that went into launching the Thai Prime-Boost trial, but it is possible to ensure that trials going forward have sufficient budgets and data management systems to be in the best position possible to answer questions about what the results mean—whatever they show.

It's not possible to unlive the miscommunications, missteps and occasional lack of commitment to authentic community engagement that have complicated several HIV prevention clinical trials. It is possible to expend the resources to do better, using the Good Participatory Practice Guidelines as a backbone for this work and recognizing that "success" may sometimes mean shelving the plans

for a study because potential trial-site communities do not want to see it done.

And it's not possible to unlive the sometimes-divisive skepticism about whether an AIDS vaccine was possible or whether money should continue to go to AIDS prevention research in the face of yawning gaps in funding for proven prevention and treatment. But it is possible to communicate how momentous the RV144 result was, how it is a strong signal that we must hold fast in the search for an AIDS vaccine and how, because this search will continue for many years, we cannot afford to cut corners on treatment and prevention that can save lives today.

Turn the page. Together, we will write the future.



**Mitchell Warren**, *Executive Director*  
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## AVAC Report 2010: Dedicated to gay men and their allies

The fight to end the AIDS epidemic is, ultimately, a fight for the rights of every human being to live with respect, dignity and health. This year, the struggle of many gay men and other men who have sex with men to secure these rights has come into stark focus. From a proposed Ugandan law seeking to punish homosexuality with the death penalty, to the criminal persecution of a gay male couple in Malawi, to large groups of anti-gay Kenyans intimidating and shutting down prevention projects working with gay men—the obstacles for gay men living freely and openly have rarely been so clear.

These repressive tactics cannot and will not staunch individual and collective efforts to raise the visibility of homosexuals living in developing and developed nations alike. Around the world, there are vibrant leaders with bold visions of a more just and open society. This year's Report is dedicated to all of the individuals and organizations engaged in the brave and necessary work of saying, "We are here. We exist. We demand our rights." We are inspired by your work, committed to your cause and proud to be your colleagues, comrades and friends.